

Dean A. Falb
Appl. No. 08/799,910

In the claims:

Please cancel claims 90-96, without prejudice.

Remarks

Claims 70, 71, 74, and 77-102 are pending and under consideration in the above-identified application.

Pursuant to the restriction requirement being made final, Applicant has herewith canceled claims 90-96 without prejudice to Applicant's right to pursue the subject matter of these claims in this or other continuing applications.

Based upon the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Rejection of Claims 70, 74, 77, 80-85, 97, 98, and 100-102 Under 35 U.S.C. § 102(a)

At page 4 of Paper No. 14, the Examiner rejects claims 70, 74, 77, 80-85, 97, 98, and 100-102 under 35 U.S.C. § 102(a) as allegedly being anticipated by Kondratyev *et al.* ("Kondratyev"). The rationale for the Examiner's rejection is set forth on pages 4-5 of Paper No.

14. In short, the Examiner contends that

Kondratyev *et al.* teach the cloning and sequencing of a radiation inducible glycosylated human early-response gene (IEX-1) which has 100% match to the polypeptide coding sequence of SEQ ID NO:9, e.g., see Fig. 2 of Kondratyev *et*

Dean A. Falb
Appl. No. 08/799,910

al., and sequence comparison generated by a database search using Smith-Waterman algorithm, nucleotide residues 1-479 of SEQ ID NO: 9. Kondratyev *et al.* also teach expression vectors, heterologous regulatory sequences operably linked to the IEX-1 mRNA, eukaryotic host cells, cDNA sequences containing a label (see materials and Methods, Figs. 1-4).

Paper No. 14 at page 4.

Applicant respectfully traverses this ground of rejection.

The Examiner is respectfully reminded of the standard for anticipation under 35 U.S.C. § 102. For a prior art reference to anticipate under 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference (*In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990)). Contrary to the Examiner's contention, Kondratyev does not teach all of the essential material compositions of claims 70, 74, 77, 80-85, 97, 98, and 100-102.

Applicant respectfully submits that Kondratyev does not teach the cloning and sequencing of a radiation inducible glycosylated human early-response gene (IEX-1) which has 100% match to the polypeptide coding sequence of SEQ ID NO: 9. Rather, Kondratyev merely discloses a radiation inducible glycosylated human early-response gene (IEX-1) which bears 98.9% identity with that of SEQ ID NO: 10. Contrary to the Examiner's contention, as Fig. 2 of Kondratyev clearly shows, the IEX-1 gene depicted in Figure 2 of Kondratyev encodes a glycine at amino acid position 54, whereas SEQ ID NO: 10 has an alanine at amino acid position 54. The corresponding nucleotide sequence triplet for the glycine at amino acid position 54 in Figure 2 of Kondratyev is "GGC" (nucleotide position 178-180), whereas the corresponding nucleotide triplet for the alanine at amino acid position 54 in SEQ ID NO: 9 is "GCC" (nucleotide position 160-162). Moreover, the IEX-1 gene depicted in Figure 2 of Kondratyev encodes an arginine at amino acid position 106, whereas SEQ ID NO: 10 has a proline at amino acid position 106.

Dean A. Falb
Appl. No. 08/799,910

The corresponding nucleotide sequence triplet for the arginine at amino acid position 106 in Figure 2 of Kondratyev is "CGG" (nucleotide position 335-337), whereas the corresponding nucleotide triplet for the alanine at amino acid position 106 in SEQ ID NO: 9 is "CCG" (nucleotide position 406-408).

Applicant respectfully submits that while it may be true that the IEX1 sequence listed as AC P46695 on the MPSRCH alignment indicates that there is 100% identity between that of IEX1 and SEQ ID NO: 10, this alleged 100% identity is apparently due to an update of the IEX1 sequence that occurred on or about July 15, 1998. This is evident from the MPSRCH alignment data provided by the Examiner for the P46695 IEX1 database sequence which indicates, at the "DT" line, that the last annotation update for the IEX1 sequence was 15-July-98. For the convenience of the Examiner, Applicant has provided herewith a copy of the MPSRCH report provided by the Examiner in connection with the previous Office Action dated May 11, 1998 (Paper No. 7) in which it is clear that, as of the then last updated annotation of November 1, 1997, the query match between SEQ ID NO: 10 and the IEX-1 sequence of Hillier *et al.* was only 98.9% (*See* Exhibit D). Applicant respectfully submits that the preliminary sequence of 156 amino acids reported by Hillier as P46695 as of the date of February 1, 1998 is in fact only 98.9% identical to the amino acid sequence of SEQ ID NO:10, and that it is only this sequence which is identical to that reported in Figure 2 of the Kondratyev publication.

As Applicant presented in the paper submitted in response to the earlier Office Action dated May 11, 1998 (Paper No. 7), according to the data base records, the complete 156 amino acid sequence that was deposited by Hillier *et al.* with the data base, as cited by the Examiner, was not made available to the public until February 1, 1998. For the convenience of the

Dean A. Falb
Appl. No. 08/799,910

Examiner, Applicant submits herewith copies of Exhibits A, B, C which were submitted with the previous response to the Office Action dated May 11, 1998 (Paper No. 7). Thus, Applicant respectfully submits that although Hillier *et al.* *eventually* disclosed a sequence which is 98.9% homologous to SEQ ID NO:10, a careful examination of the data base historical record clearly indicates that this 98.9% homologous sequence was provided by Hillier *et al.* to the data base only after the February 13, 1997 filing date of the instant application. Accordingly, in view of the above, Applicant respectfully submits that it is thus clear that the updated IEX-1 sequence information was only made available on July 15, 1998, which is well beyond the February 13, 1997 filing date of the instant application.

Accordingly, Applicant respectfully submits that the Examiner has mistakenly attributed the updated IEX-1 database sequence submitted on July 15, 1998 to be identical to that of the IEX-1 sequence reported in Figure 2 of the Kondratyev publication. Therefore, in as much as the IEX-1 sequence reported in Figure 2 of the Kondratyev publication is in fact only 98.9% identical to that of SEQ ID NO: 10, Applicant respectfully submits that claims 70, 74, 77, 80-85, 97, 98, and 100-102 cannot be anticipated by the IEX-1 sequence reported in the Kondratyev publication. Furthermore, Applicant respectfully submits that the earliest publicly available date which can be accorded the IEX1 sequence of Hillier *et al.* is that of February 1, 1998. In as much as the IEX-1 sequence of Hillier *et al.* at that date is only 98.9% identical, Applicant respectfully submits that claims 70, 74, 77, 80-85, 97, 98, and 100-102 also cannot be anticipated by the Hillier *et al.* IEX-1 sequence. Accordingly, Applicant respectfully submits that this ground for rejection is in error and should be withdrawn.

Dean A. Falb
Appl. No. 08/799,910

II. Rejection of Claims 70, 71, 74, 77, 80-87, and 97-102 Under 35 U.S.C. § 103(a)

At page 5 of Paper No. 14, the Examiner rejects claims 70, 71, 74, 77, 80-87, and 97-102 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kondratyev *et al.* (Cancer Res, 56, 1489-1502, April 1, 1996). The Examiner's rationale can be found at pages 4-6 of Paper No.

14. In short, the Examiner contends that:

The claims are drawn to SEQ ID NO: 9, expression vectors, and host cells containing SEQ ID NO: 9. Kondratyev *et al.* teach the cloning and sequencing of a radiation inducible glycosylated human early-response gene (IEX-1) which has 100% match to the polypeptide coding sequence of SEQ ID NO: 9, e.g., see Fig. 2 of Kondratyev *et al.*, and sequence comparison generated by a database search using Smith-Waterman algorithm, nucleotide residues 1-479 of SEQ ID NO: 9. While the sequence comparison shows that there are 7 mismatches between the DNA sequence of Kondratyev *et al.* and the SEQ ID NO: 9 in the intronic region (non-coding DNA sequence), it would have been obvious to one skilled in the art that the DNA sequence of Kondratyev *et al.* is an obvious variant of SEQ ID NO: 9, particularly since both sequences encode the same polypeptide sequence, and since the seven mismatches are located in the intronic region which does not affect the activity of the encoded polypeptide product. It would also have been obvious for one of ordinary skilled in the art to have employed known prokaryotic and/or eukaryotic cell lines to express the polypeptide product encoded by the IEX-1 gene for use in a glycosylation assay, as taught by Kondratyev *et al.*

Paper No 14 at pages 5-6

Applicant respectfully traverses the rejection.

For the reasons presented above in Section I on the alleged anticipation of claims 70, 71, 74, 77, 80-87, and 97-102 by either the Swiss-prot 35 data base sequence of IEX-1 of Hillier *et al.* or the IEX-1 sequence depicted in Figure 2 of Kondratyev, Applicant respectfully submits that it would not have been obvious, at the time the invention was made, to use either the partial IEX-

Dean A. Falb
Appl. No. 08/799,910

1 nucleotide sequence disclosed by Hillier on February 1, 1995 (*See Exhibit A*), the partial IEX-1 amino acid sequence disclosed on November 1, 1995 (*See Exhibit B*), the complete 98.9% identical IEX-1 sequence which was relied upon by the Examiner in the Office Action dated May 11, 1998 that was finally disclosed by Hillier *et al.* on February 1, 1998 (*See Exhibit C*) and reported in the Kondratyev publication, or the complete 100% identical IEX-1 amino acid sequence submitted by Hillier *et al.* on July 15, 1998 (*See Exhibit D*) to construct the claimed polynucleotides.

Applicant respectfully re-emphasizes that SEQ ID NO: 10 differs at two amino acid residues from the IEX-1 amino acid sequence depicted in Figure 2 of Kondratyev *et al.*: SEQ ID NO: 10 has an alanine at amino acid position 54 versus a glycine at amino acid position 54 in Figure 2 of Kondratyev *et al.*, and a proline at amino acid position 106 versus an arginine at amino acid position 106 in Figure 2 of Kondratyev *et al.*. Moreover, the biochemical properties of arginine are strikingly different than those of proline. Applicant respectfully submits that the latter amino acid difference is clearly not a conservative amino acid difference. Applicant respectfully submits that the above-identified amino acid differences between SEQ ID NO: 10 and the IEX-1 amino acid sequence depicted in Figure 2 of Kondratyev *et al.*, especially the non-conservative amino acid difference of proline for arginine at amino acid position 106 in SEQ ID NO: 10, indicate that IEX-1 is not merely an obvious variant of SEQ ID NO: 10.

Thus, Applicant respectfully submits that it would not have been obvious, at the time the invention was made, for one of ordinary skill in the art to arrive at the invention as claimed in claims 70, 71, 74, 77, 80-87, and 97-102. Applicant respectfully requests, therefore, that the

Dean A. Falb
Appl. No. 08/799,910

rejection under 35 U.S.C. § 103(a) based on the polypeptide sequences cited by the Examiner in either Figure 2 of the Kondratyev publication or the Hillier *et al.* data base sequence accorded the publicly available date of February 1, 1998, be withdrawn.

Dean A. Falb
Appl. No. 08/799,910

Conclusion

Applicant believes that each and every substantive grounds for rejection or objection has been successfully overcome or obviated and that the claims are in condition for allowance. Withdrawal of all of the rejections and objections and allowance of the application is earnestly requested. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (202) 496-4454 to discuss the same.

Respectfully submitted,

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